High Lead Exposure and Auditory Sensory-neural Function in Andean Children

S. Allen Counter,[1,2] Marie Vahter,[3] Göran Laurell,[4] Leo H. Buchanan,[5] Fernando Ortega,[6] and Staffan Skerfving[7]

[1]Department of Neurology/Biological Laboratories, Harvard University, Cambridge, MA 02138 USA; [2]Department of Physiology and Pharmacology, Karolinska Institute, Stockholm, Sweden; [3]Institute of Environmental Medicine, Karolinska Institute, Stockholm, Sweden; [4]Department of Otolaryngology, Karolinska Hospital, Karolinska Institute, Stockholm, Sweden; [5]Department of Audiology, Shriver Center/Harvard University Health Services, Waltham, MA 02154 USA.; [6]Department of Medicine, Universidad San Francisco De Quito, Quito, Ecuador; [7]Department of Occupational and Environmental Medicine, University Hospital, Lund, Sweden

We investigated blood lead (B-Pb) and mercury (B-Hg) levels and auditory sensory-neural function in 62 Andean school children living in a Pb-contaminated area of Ecuador and 14 children in a neighboring gold mining area with no known Pb exposure. The median B-Pb level for 62 children in the Pb-exposed group was 52.6 μg/dl (range 9.9–110.0 μg/dl) compared with 6.4 μg/dl (range 3.9–12.0 μg/dl) for the children in the non-Pb exposed group; the differences were statistically significant ($p<0.001$). Auditory thresholds for the Pb-exposed group were normal at the pure tone frequencies of 0.25–8 kHz over the entire range of B-Pb levels. Auditory brain stem response tests in seven children with high B-Pb levels showed normal absolute peak and interpeak latencies. The median B-Hg levels were 0.16 μg/dl (range 0.04–0.58 μg/dl) for children in the Pb-exposed group and 0.22 μg/dl (range 0.1–0.44 μg/dl) for children in the non-Pb exposed gold mining area, and showed no significant relationship to auditory function. Key words: auditory, brain stem evoked response, hearing, lead, mercury. Environ Health Perspect 105:522–526 (1997)

Lead (Pb) is a well-known neurotoxic agent that may cause severe impairment of nerve tissue, particularly in the developing central nervous system (CNS) (1). A number of medical studies have suggested damage to the CNS in the developing fetus, resulting in impairment of cognitive function and the induction of behavioral disorders in young children with blood lead (B-Pb) levels of about 10.0 μg/dl or higher (2–4). Plumbism (lead poisoning) has also been associated with reduced gestational age and birth weight, hypertension, lower hemoglobin levels, and impairment of renal function (5,6). Pb poisoning remains a major problem in some industrialized countries, such as the United States, where B-Pb concentrations of ≥10.0 μg/dl can still be found in 8.9% of minority and low-income children (7). Some recent studies have reported sensory-neural hearing impairment at the cochlear and brain stem levels in Pb-exposed children and occupationally exposed workers at B-Pb levels of <10.0 μg/dl (8–11). If, as these investigations suggest, sensory-neural hearing impairment is a feature of childhood plumbism, it is likely to contribute to the observed cognitive disorders attributed to Pb exposure, particularly when the B-Pb level is high.

We investigated B-Pb levels and auditory sensory-neural functioning in children living in an area of high Pb use in Cotapaxi Province, Ecuador, where Pb-glazing of ceramic tiles and artisan crafts is the main cottage industry. The primary source of Pb exposure in the area is contact with Pb

extracted from discarded automobile batteries. The Pb and other metals are extracted manually from automobile and standard utility batteries, mixed with water, and churned either by hand or motorized stirring device until the mixture is in suspended form. The suspended Pb mixture, which is stored in nearby open vats, is then poured by hand onto the ceramics that are baked in large, mainly sawdust-fueled kilns at high temperature (≈ 1200°C) to produce a smooth, more durable, and cosmetically appealing surface. The resultant dark heavy smoke and particles discharged from the top of the open ovens are released unfiltered through open vents into the environment. Such ovens and the vats of lead in suspension are seen throughout the villages of La Victoria and El Tejar, Ecuador, at many of the residences. We also measured the blood levels of mercury (a component of some utility batteries) in children living in the Pb producing area. B-Pb and blood mercury (B-Hg) levels were measured in a second region of the province that has no Pb production, but where the use of Hg is common in gold mining operations that release elemental Hg into the local rivers and fishing tributaries. The resultant methylmercury (MeHg) exposure from contaminated fish may have neurotoxic consequences and impair the peripheral and central auditory systems (12,13).

The aims of this study were to investigate Pb and Hg exposure levels and auditory sensory-neural functioning in Ecuadorian

children living in a Pb-tile glazing area and a gold mining area, and to report the findings to the local communities and health authorities. The specific research study questions investigated were 1) What are the Pb and Hg exposure levels in children living in the Pb producing area and in a comparable area of no known lead production where Hg is used in gold mining? 2) Is there a correlation between B-Pb, B-Hg, and sensory-neural hearing loss? 3) Is nerve conduction in the brain stem auditory pathways altered by elevated Pb or Hg levels?

Methods

Subjects and locations. Blood levels of Pb and Hg were investigated in 82 Andean school children aged 4–15 years (Pb-exposed group) who live in the ceramic tile production and Pb-glazing villages of La Victoria and El Tejar, in Pujilí county, Cotapaxi Province, Ecuador, at an altitude of approximately 2,850 m. Many of the children were of indigenous Quichua background. The combined population of La Victoria and El Tejar is 2,648 (1,390 females and 1,308 males). The children in the Pb-exposed group (40 males and 42 females) were selected randomly from several classrooms and grade levels with the assistance of the school principal, teachers, and parents, and provided an epidemiological profile of the study area. Since most villagers have tile baking ovens in close proximity to their homes, it

may be assumed that most children in the area have a high risk of Pb exposure. B-Pb and B-Hg were measured in a second group of school children (*n* = 14: 5 males and 9 females aged 5–14 years) living in a nontile producing area (non-Pb-exposed group) approximately 100 km from the Pb-exposed group study site. The non-Pb-exposed group was located on the western slope of the Andes, at an altitude of about 700 m, in La Mana, Ecuador. The inhabitants of the La Mana area are of mainly mixed (mestizo) ethnic background and the primary occupations in this region are farming and gold mining. Mercury is used in the La Mana area in the gold mining process. Because Hg is a component of the battery extract used in the Pb glazing area and widely used in the gold mining areas, B-Hg levels were also measured in both groups.

Nutritional background. The basic diet of the population of La Victoria and El Tejar (Pb-exposed group) consists mainly of corn, barley, wheat bread, potatoes, cheese, rice, and some pasta, milk, vegetables, chicken, pork, and guinea pig. Because of a previous history of iodine deficiency in the area, local consumer salt supplemented with iodine was introduced about 10 years ago. In the La Mana region, the diet of the population (non-Pb-exposed group) mainly consists of plantain, rice, manioc, bananas, beans, a few vegetables, a small amount of meat, and fish from the nearby river Calope, which receives water from several streams serving gold mines in the area.

Blood tests. Metal exposure was assessed by determination of the concentration of Pb and Hg in whole blood. Blood was collected from the cubital vein following thorough skin cleaning using two or three swabs containing isopropanol. Blood (10–20 ml) was collected using evacuated blood-collecting tubes with Li-heparin. A suitable number of tubes from the same batch was previously tested to ensure freedom from metal contamination. Quality control tests were performed for both Pb and Hg samples. Determination of Pb and Hg in blood was carried out using inductively coupled plasma-mass spectrometry (ICPMS). Briefly, 4.5 ml of a solution of EDTA (0.5 g/l), Triton-X 100 (0.5 g/l), and ammonia (5 g/l) in Millipore water was added to 0.5 ml of blood. Each dilution was spiked to 20 µg/dl with bismuth (Bi) and indium (In). The samples were shaken and then analyzed by ICPMS equipment (VG PlasmaQuad, PQ2 Plus, Fisons Elemental, Winsford, Cheshire, U.K.) in a segmented flow mode, three readings of each isotope (determined in a peak jumping mode, 3 points/peak) repeated more than 10 times during 10 sec acquisition ([206]Pb, [207]Pb, [208]Pb, and [202]Hg). The sum of the Pb isotope

readings was used, [209]Bi and [115]In (International Standards), and [118]Sn (for interference control). Internal and external quality control samples for Pb and Hg in blood were analyzed with the collected samples. Small samples of hair were collected from children and adults in the La Mana region as an additional means of testing for Hg exposure levels. The external quality control for the blood Pb analysis included spiked cow blood (12 samples, lab values = 1.009x, reference values= -0.19). The quality control for blood Hg involved analysis of the reference materials Seronorm B 203056 and B 205053 (Seronorm Trace Elements, Nycomed AS, Oslo, Norway). Human hair reference material from the Peoples Republic of China (CRM GBW 09101) was used for quality control for hair samples examined in this study.

Otolaryngologic examinations and audiologic tests. An otologic/audiologic case history was taken on each subject/patient at the time of examination. An otoscope was used for diagnostic examination of the ear canal, eardrum, and middle ear. Tympanometric results were obtained using the GSI-37 tympanometer. Tympanometry, in combination with the otolaryngologic examination, was used to rule out eustachian dysfunction, eardrum abnormalities, otitis media, ossicular chain disruption, and other middle-ear pathology. Only children without sign of middle-ear pathology were included in this aspect of the study. Audiologic test data were obtained from 62 of the 82 children in the Pb-exposed group who received blood tests. Thirteen subjects were unavailable for audiologic examination because of work or school schedules, and data were not included for seven subjects because of complications from chronic otitis media, tympanic membrane injury, genetic deafness, and unreliable responses. The 62 Pb-exposed children from whom audiologic data were obtained ranged in age from 6 to 15 years (median age 10 years). Pure tone air conduction threshold data were obtained in a quiet classroom or other sound-attenuated setting at 0.25, 0.5, 1, 2, 3, 4, 6, and 8 kHz using the Interacoustics (Model AD 12, Copenhagen, Denmark) and the Tegner (Model PTA 8, Stockholm, Sweden) portable audiometers with standard TDH 39 and 49 earphones (calibrated to the ISO 389 standards). Biological calibration checks of the instruments were performed regularly on the normal-hearing staff. Bone conduction thresholds were obtained on the AD 12 at 0.25, 0.5, 1, 2, and 4 kHz if a hearing loss was detected. Pure tone thresholds were obtained using the conventional descending-ascending threshold crossing technique. Threshold was defined as the minimum decibel (dB) level at which the participant responded at least two

times on ascending trials. Intratest reliability was ± 5 dB at 1 kHz. All participants responded by raising their hands when a tone was heard. Pure tone threshold data were analyzed for each ear of the 62 participants for all test frequencies (0.25–8 kHz). All audiologic data [case histories, pure tone thresholds, auditory brain stem response (ABR), tympanometry] were used in data interpretation. Thresholds at five frequencies (2, 3, 4, 6, and 8 kHz) were averaged for all subjects to assess high-frequency hearing sensitivity. Standard statistical tests, including the mean, standard deviation, median and range, *t*-tests, and the Pearson correlation coefficients were used for analysis of statistical relations between B-Pb, B-Hg, and auditory sensitivity.

ABR tests. ABR testing was performed on seven subjects (ages 5–15 years) with a Medelec/GSI 50 (Milford, NH) evoked response averaging computer. The subjects were selected on the basis of recommendations for ABR by the audiologist and otolaryngologist because of atypical responses to audiological testing or suspected auditory-neurological involvement. The average time required for a complete ABR test with repeated recordings for reliability was 1 hr from the electrode placement to the hard copy result printout. For all ABR measurements, the scalp, forehead, and ear lobes were cleaned thoroughly with swabs containing isopropanol, and gold-plated cup electrodes were placed at C_z (vertex +), A_1, A_2, and Fpz (frontal pole, saggital plane) according to the 10–20 International Electrode System *(14)*. The electrodes were connected to a standard (100–3,000 Hz bandpass filters) pre amp (10^5), which was connected to the computer averager. Broad band monaural rarefaction click stimuli (70–100 dB normalized hearing level, 100-µsec duration) were delivered to the ear through TDH 49 headphones at a rate of 10/sec for the ABR tests (1,024–2,048 sweeps/trial). The absolute latencies of waves I, II, III, IV, V, and the interwave latencies of I-III, III-V, and I-V were measured in milliseconds and analyzed for mean and variability (16 measures per subject). Wave form morphology was examined in relation to a standardized ABR template *(14)*.

Results

B-Pb levels. The median B-Pb level for the 82 children tested in the Pb-tile glazing villages of La Victoria and El Tejar (Pb-exposed group) was found to be 50.6 µg/dl (range 9.9–110.0 µg/dl). In the non-Pb-exposed group (control area), the children had a median B-Pb level of 6.4 µg/dl (range 3.9–12.0 µg/dl, *n* = 14). The median B-Pb level of the 62 children receiving

audiologic tests in the Pb-exposed group was 52.6 µg/dl (range 9.9–110.0 µg/dl), comparable to that of the total sample of 82 subjects in the epidemiological profile. The difference in B-Pb levels between children in the Pb-exposed group and those in the non-Pb-exposed group was statistically significant ($p<0.001$). There was no statistically significant relationship between B-Pb level and age of the children in either the Pb-exposed group or the non-Pb-exposed group, nor was there any statistically significant difference in B-Pb levels between boys and girls (medians were 53.0 and 41.0 µg/dl for the Pb-exposed group and 5.0 and 7.1 µg/dl for the non-Pb-exposed group for boys and girls, respectively).

Audiologic/otolaryngologic findings. Figure 1 shows the distribution of B-Pb levels for the 62 children receiving audiologic tests. Otolaryngologic examination of 82 children in the Pb-exposed group revealed one case of otitis media, one case of tympanic perforation, and no atresia or nasopharyngeal abnormality. The mean auditory threshold obtained from 62 children at the pure tone frequencies 0.25, 0.5, 1, 2, 3, 4, 6, and 8 kHz was in the normal range (10–24 dB hearing level). A small number of individuals showed slightly elevated auditory thresholds at some pure tone frequencies, but statistical analyses using Pearson's r coefficient revealed no significant relationship between B-Pb levels and hearing acuity. Figure 2 shows the auditory thresholds for 62 individual subjects with B-Pb levels ranging from 9.9 µg/dl to 110.0 µg/dl at the pure tone frequencies of 1–8 kHz. Figure 3A illustrates the averaged high frequency threshold at 2, 3, 4, 6, and 8 kHz (the frequency range of previously reported Pb-induced hearing impairment and the frequency range of specific sensitivity to ototoxicity) as a function of B-Pb level. Figure 3A demonstrates normal auditory sensitivity at moderate and high B-Pb levels. Of the 82 children in the Pb-exposed group tested for B-Pb levels, 57 children who indicated that their families were actively involved in Pb glazing activities had a median B-Pb level of 60.0 µg/dl (range 12.0–110.0 µg/dl), whereas 25 children who indicated no active family involvement in Pb glazing had a median B-Pb level of 21.0 µg/dl (range 9.9–87.0 µg/dl). Among the 62 children who received audiological tests, 46 children whose families were actively involved in Pb glazing showed a median B-Pb level of 59.1 µg/dl (range 11.8–110.0 µg/dl), whereas 15 children who indicated no active Pb glazing at their homes had a median B-Pb level of 18.9 µg/dl (range 9.9–87.2 µg/dl) (no information was available on 1 child). The differ-
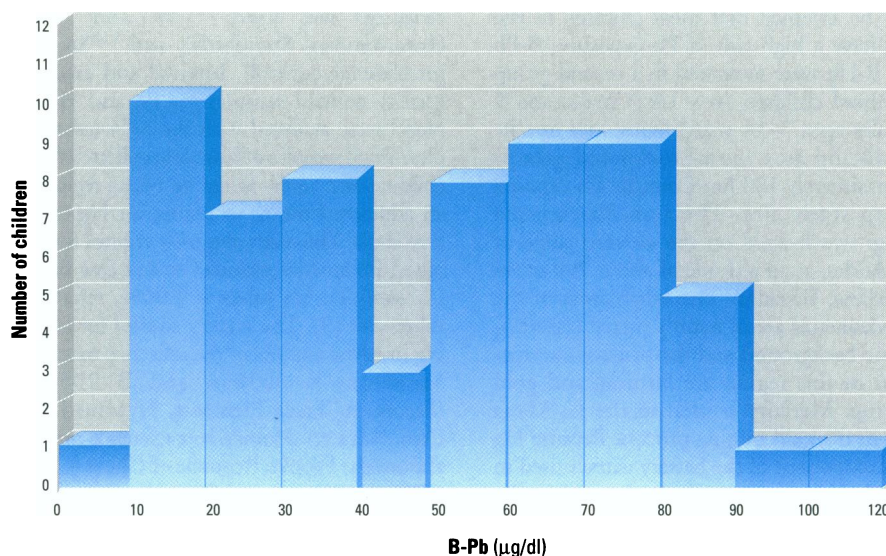
Figure 1. Distribution of blood lead (B-Pb) levels for the 62 Andean children from the Pb-glazing ceramic tile production villages of La Victoria and El Tejar, Ecuador (Pb-exposed group) who received audiologic tests.

ences in B-Pb levels between the 46 children who reported active family involvement in Pb production and the 15 who indicated no active involvement was statistically significant ($p = 0.001$).

B-Hg levels. The median B-Hg concentration for 82 children in the Pb-exposed group was 0.16 µg/dl (range 0.04–0.58 µg/dl)(Table 1). The median B-Hg level for children in the non-Pb-exposed group from the gold mining area was 0.22 µg/dl (range 0.10–0.44 µg/dl). For hair samples, the measured B-Hg level (MeHg) was 0.3 µg/g (range ≤0.2–1.3 µg/g) for children in the non-Pb-exposed group (Table 1). The median value for the 62 children receiving audiologic tests was 0.16 µg/dl (range 0.04–0.58 µg/dl)(Table 1). The averaged high frequency auditory threshold at 2, 3, 4, 6, and 8 kHz for the 62 children measured as a function of B-Hg level indicated no correlation between B-Hg and hearing acuity for either ear in the Pb-exposed Group (Fig. 3B).

ABR. In the Pb-exposed group, electrophysiologic brain stem tests on seven children with suspected neuro-audiologic involvement and B-Pb levels of 64.8, 70.0, 70.8, 71.1, 71.1, 79.5, and 83.3 µg/dl revealed ABR recordings in the normal range for absolute (I-V) and interwave peak (I-III, III-V, and I-V) latencies (Table 2). The interpeak latencies or neural conduction times ranged from 2.07 to 2.18 msec for wave peaks I-III, 1.48 to 1.95 msec for III-V, and 3.55 to 4.06 msec for I-V.
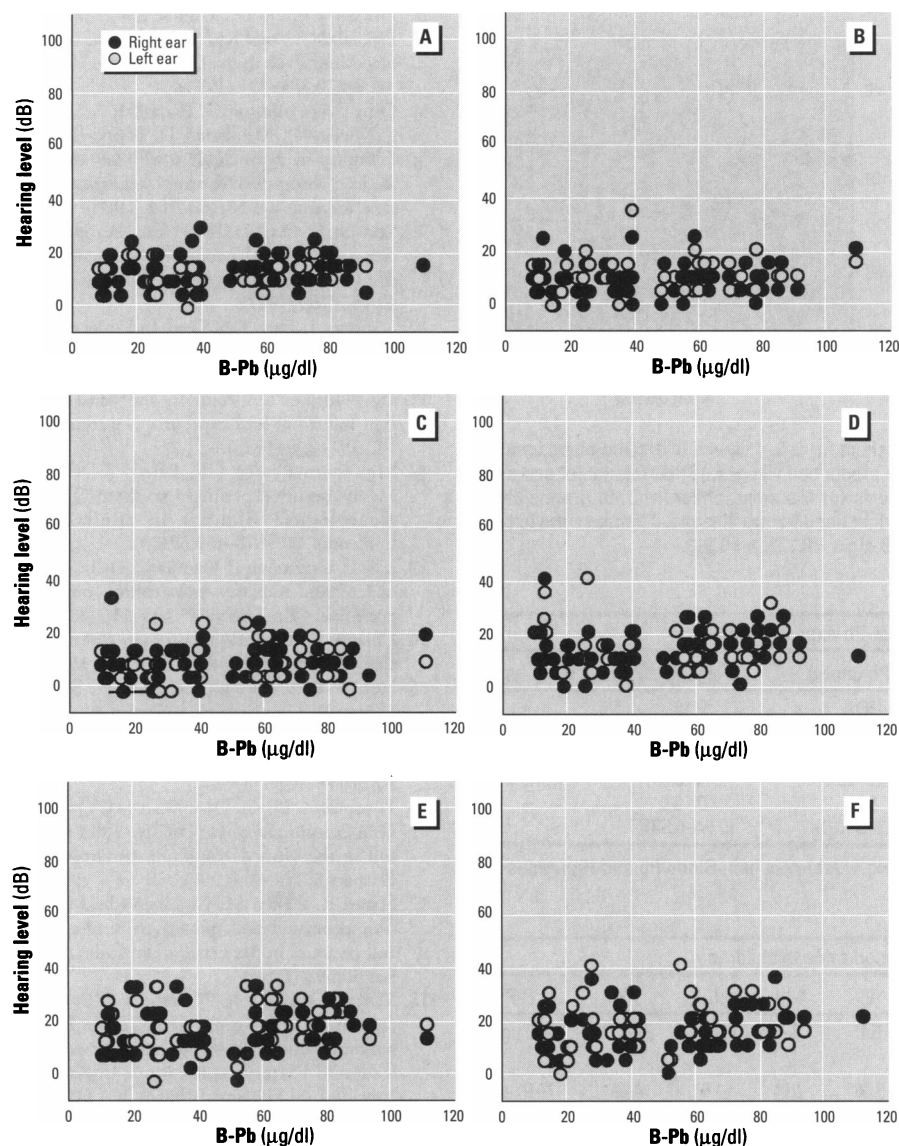
Discussion

The median B-Pb level found among children exposed to Pb from automobile batter-

ies in the villages of La Victoria and El Tejar, Ecuador, was found to be approximately 10 times higher than in the children of comparable age in a nonlead producing area of Ecuador, and was comparable to the occupational exposure limits recommended for adult male workers in some countries.

The observation of low B-Hg in the children of the Pb-exposed group indicates minimal exposure to Hg contaminants in the battery extract used for glazing. This finding further indicates that the absorption of Pb is more of a health risk than the other extracted metals used in the tile glazing process. The low B-Hg levels in the non-Pb-exposed group of La Mana (Punta Brava and Calope de Garrido) suggests the absence of any significant MeHg exposure from the consumption of contaminated fish from the local river (Rio Calope), which may receive Hg residues from upstream gold mining operations.

The findings of this study do not support the hypothesis of a relationship between sensory-neural hearing loss and elevated B-Pb levels in children. The observation of normal hearing acuity in a group of 62 children with moderate to extremely high B-Pb levels strongly suggests the absence of any effect of Pb intoxication on the auditory end-organ and contradicts some previous reports. Thus, previous findings of a linear relationship between B-Pb levels and hearing thresholds at considerably lower B-Pb levels may be the result of statistical, sampling, or testing errors. The findings of the present study further suggest that the cognitive disorders associated with childhood plumbism are not necessarily related to impaired hearing acuity.

The results of the electrophysiologic

earlier preliminary screening of 10 children from the same geographic area, who worked in the Pb-glazing process for up to 3 years, indicated B-Pb levels in excess of 20.0 µg/dl in all subjects tested *(17)*.

The findings of this study among rural Andean children are similar to some previous studies that have reported Pb poisoning among children from exposure to Pb particles from automobile battery repair shops *(18)* and from recycling exhausted batteries or burning battery casings for home heat *(19)*. This study, however, focused uniquely on the widespread lead-glazing and baking of ceramic tiles and artisan projects, which continues to put an entire village population at risk. The B-Pb levels observed on this substantial sample of Andean children are considerably higher than those reported in most population surveys, and more elevated than levels generally believed to be associated with sensory and cognitive disorders *(4,5,8,9,11)*. For comparison, it may be noted that the average B-Pb level for children of comparable age in the United States ranges from 2.8 to 5.6 µg/dl and in Sweden from 2.2 to 2.9 µg/dl *(7,20–22)*.

Although the current study did not find a correlation between high Pb exposure and auditory function, the previously reported risks for other severe health hazards from extensive Pb poisoning make it imperative to decrease the present levels of Pb contamination in the Pb-glazing tile-producing areas of Ecuador. Most likely, there is a general Pb contamination of the area, e.g., in the soil. Since most of the families in the tile-glazing cottage industry customarily earn their living from this activity, there are no simple means of immediately decreasing the exposure levels substantially.

It is recommended that a program be developed for B-Pb screening and follow-up of all children in the geographic area of the ceramic tile lead-glazing industry. Also, a program for suitable environmental intervention and medical management should be developed in close cooperation with local health authorities and community leaders. Identification of the routes of exposure, possible modification of the glazing process or use of alternative glazing compounds in order to minimize the contact with Pb, installation of protective measures wherever possible, and periodic information to families at risk for Pb exposure should be a part of such a program. Children and women of childbearing age should be discouraged from engaging in Pb tile-glazing production. Additional tests should be conducted on children and adults in the Pb-glazing areas to determine the general neurological, cognitive, and physiological effects of elevated

Figure 2. Auditory thresholds for each of 62 children from the Pb-glazing ceramic tile production area (Pb-exposed group) of Ecuador at the pure tone frequencies 1 kHz (A), 2 kHz (B), 3 kHz (C), 4 kHz (D), 6 kHz (E), and 8 kHz (F) for the right and left ears. B-Pb, blood lead.

brain stem tests offer further objective evidence of the absence of an elevated B-Pb effect on the cochlea, neurons of the auditory nerve, or the more central brain stem tracts and nuclei. Previous studies have reported consistent linear increases in the absolute latencies of waves III and V, which are believed to be generated at the levels of the nucleus of the lateral lemniscus and the inferior colliculus, respectively, with increases in B-Pb *(15)*. The ABR results of this study, however, showed normal synaptic latencies and internuclear conduction time in subjects with very high B-Pb levels. The normal ABR absolute and interwave peak latencies in some children with elevated B-Pb levels suggest that the effects of Pb on the brain stem tracts and nuclei are minimal or inconsistent

at best, and possibly influenced by other factors such as the onset, duration, and frequency of Pb exposure, as well as diseases other than childhood plumbism. More extensive ABR testing on a larger group of Pb-exposed subjects and with variations of stimulus parameters is needed before any firm conclusion can be reached regarding neuroauditory impairment and B-Pb levels.
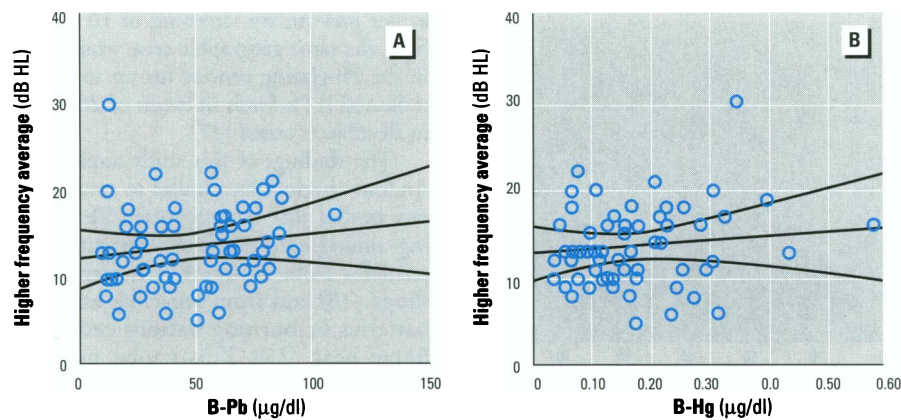
The high B-Pb levels found in the children of La Victoria and El Tejar probably result from ingestion of Pb-contaminated soil and household dust and Pb-contaminated hands and toys, food, and drinking water *(16)*. It is also probable that most of the children have experienced lifelong exposure to Pb, since tile production has been common in the area for at least the past 20 years. An

Figure 3. (A) Correlation of averaged high frequency threshold for 2, 3, 4, 6, and 8 kHz and blood lead (B-Pb) levels for 62 children from the Pb-glazing ceramic tile production villages; (B) correlation of averaged high frequency threshold and blood mercury (B-Hg) levels for the same children. Both graphs show regression lines at the 95% confidence interval. Only the right ear data are illustrated because the left ear results were similar. For B-Pb, $r = 0.141$, $p = 0.275$ and for B-Hg, $r = 0.122$, $p = 0.343$. dB HL, decibel hearing level.

Table 1. Median B-Pb, B-Hg, and H-Hg levels in Pb and non-Pb-exposed subjects

	B-Pb (µg/dl)	B-Hg (µg/dl)	H-Hg (µg/g)
Total Pb-exposed group children ($n = 82$)	50.6 (9.9–110.0)	0.16 (0.04–0.58)	–
Total non-Pb-exposed group children ($n = 14$)	6.4 (3.9–2.0)	0.22 (0.10–0.44)	0.3 ($\leq$0.02–0.13)
Pb-exposed children with audiologic data ($n = 62$)	52.6 (9.9–110.0)	0.16 (0.04–0.58)	–

Abbreviations: B-Pb, blood lead; B-Hg, blood mercury; H-Hg, mercury in hair. Blood Pb and Hg ranges are enclosed in parentheses.

Table 2. Auditory brain stem responses (ABRs) in Pb-exposed Andean children

Wave peak	I	II	III	IV	V	I-III	III-V	I-V	B-Pb
Normal mean values (msec)[a]	1.58	2.62	3.62	4.71	5.1	1.8–2.4	1.3–2.03	3.6-4.2	(<10 µg/dl)
Subject 1 (age 9)	1.60	2.57	3.75	5.03	5.66	2.14	1.91	4.06	70.8 µg/dl
Subject 2 (age 10)	1.79	2.85	3.86	5.45	5.58	2.07	1.71	3.78	83.3 µg/dl
Subject 3 (age 5)	1.75	2.85	3.86	5.11	5.82	2.10	1.95	4.06	71.1 µg/dl
Subject 4 (age 15)	1.64	2.73	3.78	5.00	5.50	2.14	1.71	3.86	71.1 µg/dl
Subject 5 (age 11)	1.60	2.77	3.75	4.92	5.50	2.14	1.75	3.90	64.8 µg/dl
Subject 6 (age 14)	1.85	2.96	4.02	5.23	5.50	2.07	1.48	3.55	70.0 µg/dl
Subject 7 (age 10)	1.48	2.61	3.67	5.03	5.42	2.18	1.75	3.94	79.5 µg/dl

B-Pb, blood lead.
[a]ABR normal mean values are standard and conform to clinical normal values on the ABR test equipment used.

B-Pb levels on the population. The findings of this study were reported to the local communities and local health authorities.

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